PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 : A61K 31/56 // (A61K 31/56 A61K 31:415)	A1	(11) International Publication Number: WO 92/14472
		(43) International Publication Date: 3 September 1992 (03.09.92)

(21) International Application Number: PCT/EP92/00364

(22) International Filing Date: 21 February 1992 (21.02.92)

(30) Priority data:
9103764.8 22 February 1991 (22.02.91) GB

(71) Applicant *(for all designated States except US)*: GLAXO GROUP LIMITED [GB/GB]; Glaxo House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)* : HILL, Ernest, Arthur [GB/GB]; Glaxo Manufacturing Services Limited, Harmire Road, Barnard Castle, County Durham D112 8DT (GB).

(74) Agents: BREWER, Christopher, Laurence et al.; Glaxo Holdings p.l.c., Glaxo House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).

(81) Designated States: AT, AT (European patent), AU, BB, BE (European patent), BF (OAPI patent), BG, BJ (OAPI patent), BR, CA, CF (OAPI patent), CG (OAPI patent), CH, CH (European patent), CI (OAPI patent), CM (OAPI patent), CS, DE, DE (European patent), DK, DK (European patent), ES, ES (European patent), FI, FR (European patent), GA (OAPI patent), GB, GB (European patent), GN (OAPI patent), GR (European patent), HU, IT (European patent), JP, KP, KR, LK, LU, LU (European patent), MC (European patent), MG, ML (OAPI patent), MN, MR (OAPI patent), MW, NL, NL (European patent), NO, PL, RO, RU, SD, SE, SE (European patent), SN (OAPI patent), TD (OAPI patent), TG (OAPI patent), US.

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: COMPOSITIONS FOR TOPICAL ADMINISTRATION CONTAINING FLUTICASONE PROPIONATE AND OXICONAZOLE OR ITS SALTS

(57) Abstract

A method for the treatment of skin disorders comprising the topical administration of fluticasone propionate and oxiconazole or a physiologically acceptable salt thereof and pharmaceutical formulations adapted for topical use and comprising fluticasone propionate, oxiconazole or a physiologically acceptable salt thereof and a pharmaceutically acceptable carrier are disclosed.

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COMPOSITIONS FOR TOPICAL ADMINISTRATION CONTAINING FLUTICASONE PROPIONATE AND OXICONAZOLE OR ITS SALTS

The present invention relates to topical pharmaceutical compositions containing fluticasone propionate and oxiconazole as active ingredients.

Fluticasone propionate is the approved name for (S-fluoromethyl 6a,9a-difluoro-11b-hydroxy-16a-methyl-17a-propionyloxy-3-oxandrosta-1,4-diene 17b-carbothioate), which is disclosed in United Kingdom Patent Specification No. 2088877. Fluticasone propionate is a corticosteroid having good topical anti-inflammatory activity with minimal liability to cause undesired systemic side effects.

Oxiconazole is the approved name for 1-(2-(4-chlorophenyl)-2-[(2,4-dichlorophenyl)methoxyimino)ethyl)-1H-imidazole. Oxiconazole has antifungal and antibacterial actions.

Topical corticosteroids are widely used for the treatment of inflammatory skin conditions such as, for example, inflammatory dermatoses and eczemas. There are many skin conditions such as, for example, infected dermatoses and eczema wherein infection by gram positive bacteria especially Staphylococci aureus and Streptococcus species and/or fungi, such as dermatophytes, yeasts and moulds, co-exist with inflammation.

We have now found that a combination of fluticasone propionate and oxiconazole is particularly effective in the treatment of skin disorders wherein inflammation and infection by bacteria and/or fungi coexist.

The invention thus provides a method of treating skin disorders which comprises the topical administration to an animal, including a human, of fluticasone propionate and oxiconazole or a physiologically acceptable salt thereof.

It will be appreciated that reference to treatment is intended to include prophylaxis as well as the alleviation of established symptoms.

Suitable physiologically acceptable salts of oxiconazole include the hydrochloride, sulphate and nitrate salts. Preferably oxiconazole will be in the form of its nitrate.

According to a further aspect the invention provides topical pharmaceutical compositions comprising fluticasone propionate and oxiconazole or a physiologically acceptable salt thereof.

Compositions according to the invention can conveniently be formulated in conventional manner using one or more pharmaceutically acceptable carriers or excipients. Such compositions may take the form of, for example, ointments, lotions, creams, powders, drops (e.g. eye or ear drops) or sprays. Preferably the compositions of the invention will be in the form of creams or ointments.

Ointments may normally be prepared by melting white soft paraffin, (white petrolatum) incorporating any additives e.g. surfactants and solvents, and blending in a slurry of the drug in a minimum quantity of liquid paraffin. The melt is then cooled under controlled conditions and stirred until solidification occurs.

Creams may normally be prepared by combining the oily phase of an ointment as a melt as described above, with suitable oil and water soluble surfactants and an aqueous phase containing the drug and suitable anti-microbial preservatives, homogenising to form the cream and stirring gently until cool.

Compositions according to the invention will generally contain additional excipients, for example preservatives (such as benzoic acid), emulsifying agents (such as polysorbates, e.g. polysorbate 60), and viscosity enhancing agents (such as cetostearyl alcohol).

It is an advantage of the compositions of the present invention that, due to their improved effectiveness, they generally need be applied only once or twice daily. This is in contrast to known combined therapies comprising a corticosteroid and an antibacterial and/or antifungal agent, which all require multiple daily applications.

The amount of fluticasone propionate contained in the compositions of the invention will depend on the particular type of formulation concerned but will generally be in the range of from 0.0005% to 1.0% by weight of the formulation, preferably about 0.05% w/w.

The amount of oxiconazole in the compositions will also depend on the particular formulation but the content of free base will generally be in the range of from 0.01 to 10.00% by weight of the formulation, preferably about 1.00% w/w.

The invention is further illustrated by the following non-limiting example :

Example 1

	% w/w
Oxiconazole Nitrate	1.147 *
Fluticasone Propionate (micronised)	0.05
Cetostearyl Alcohol	10.00
White Soft Paraffin	10.00
Polysorbate 60	2.50
Propylene Glycol	10.00
Benzoic Acid	0.20
Purified Water	to 100.00

* equivalent to 1.00% oxiconazole base.

Claims

1. A method of treating skin disorders in an animal including man comprising the topical administration fluticasone propionate and oxiconazole or a pharmaceutically acceptable salt thereof.

2. A method according to Claim 1 wherein the fluticasone propionate and oxiconazole or pharmaceutically acceptable salt thereof are administered sequentially.

3. A method according to Claim 1 wherein the fluticasone propionate and oxiconazole or pharmaceutically acceptable salt thereof are administered simultaneously.

4. A method according to any one of Claims 1 to 3 wherein the oxiconazole is present as oxiconazole nitrate.

5. A method as claimed in any one of Claims 1 to 4 wherein the ratio of fluticasone propionate to oxiconazole is about 0.05:1.00% w/w.

6. A pharmaceutical formulation adapted for topical administration and comprising fluticasone propionate, oxiconazole or a pharmaceutically acceptable salt thereof and pharmaceutically acceptable carrier therefor.

7. A pharmaceutical formulation according to Claim 6 wherein oxiconazole is present as oxiconazole nitrate.

8. A pharmaceutical formulation according to Claim 6 or Claim 7 in the form of an ointment, lotion, cream, powder, drops or sprays.

9. A pharmaceutical formulation as claimed in any one of Claims 6 to 8 wherein the fluticasone propionate is present in an amount of from 0.0005% to 1% by weight and the oxiconazole is present in an amount of 0.01 to 10.00% by weight.

10. A pharmaceutical formulation as claimed in any one of Claims 6 to 9 wherein the fluticasone propionate is present in an amount of about 0.05% w/w and the oxiconazole is present in an amount of about 1.00% w/w based upon the free base.

INTERNATIONAL SEARCH REPORT

International Application PCT/EP 92/00364

I. CLASSIFICATION OF SUBJECT MA[redacted] (if several classification symbols apply, indicate all)[6]

According to International Patent Classification (IPC) or to both National Classification and IPC

Int.Cl.5 A 61 K 31/56 //(A 61 K 31/56 A 61 K 31:415)

II. FIELDS SEARCHED

Minimum Documentation Searched[7]

Classification System	Classification Symbols
Int.Cl.5	A 61 K

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched[8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT[9]

Category °	Citation of Document,[11] with indication, where appropriate, of the relevant passages[12]	Relevant to Claim No.[13]
A	Weekly Pharmacy Reports: "The Green Sheet", vol. 40, no. 1, 7 January 1991, "Glaxo's cultivate (fluticasone propionate) ointment and cream approved as twice daily", pages 2,3, see publication	1-10

° Special categories of cited documents :[10]

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IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
17-06-1992	16.07.92
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	D. Fras

Form PCT/ISA/210 (second sheet) (January 1985)